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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LAM, ANN Y	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 12/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/768,742	TERPETSCHNIG ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-30,33-41,83,84 and 88-90* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-30,33-41,83,84 and 88-90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Claims 83, 28, 30, 37-41, 88, 89 and 90 are rejected under 35 U.S.C. 102(e) as being anticipated by Pollok et al., 6,410,255.

As to claim 83, Pollok et al. disclose a kit comprising:

an enzyme (i.e., protease, col. 25, line 9);

a luminophore (i.e., fluorescent moiety, col. 25, line 6) bound to a substrate (i.e., polypeptide moiety, col. 25, lines 4-6) for the enzyme ;

and a particulate mass label including a bead (i.e., solid matrix; e.g., bead, col. 25, lines 30-32) distinct from the enzyme and capable of specifically binding to the substrate or a product of the substrate produced by action of the enzyme on the substrate, but not both (col. 25, lines 30-36);

wherein a luminescence property of the luminophore is sensitive to binding of the mass label to the substrate or product (col. 25, lines 30-36).

As to claim 28, the luminophore is photoluminescent (col. 25, line 6.)

As to claim 30, the luminophore is bound to the substrate noncovalently (col. 20, lines 64-67.)

As to claim 37, the luminophore is not normally present in the sample. (The Office notes that this is a recitation of intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, such as in this case, then it meets the claim.)

As to claim 38, the mass label is not normally present in the sample (The Office notes that this is also a recitation of intended use, and the prior art structure is capable of performing the intended use.)

As to claim 39, the property of the luminophore is related to a rotational diffusion coefficient of the probe (col. 25, lines 30-36.)

As to claim 40, the property may be measured using a technique selected from the group consisting of polarization and light scattering (col. 25, lines 30-36).

As to claim 41, the property of the luminophore is related to the translational diffusion coefficient of the robe (col. 25, lines 30-36.)

As to claim 88, the mass label (bead, col. 25, line 32) is capable of binding specifically to the product (which is deemed to be the remainder of the polypeptide once it is cleaved by a protease; col. 25, lines 3-6 and lines 33-36), and the luminescence property of the luminophore is different for the luminophore bound to the substrate than for a complex of the luminophore, the product, and the mass label (see col. 25, lines 33-

36, disclosing that cleavage of the optical probe, comprising the polypeptide, results in a larger drop in fluorescence polarization because of the increased rotational flexibility of the optical probe once separated from the bead).

As to claim 89, the luminescence property may be measured using fluorescence polarization (col. 25, lines 30-36.)

As to claim 90, the enzyme converts the luminophore bound to the substrate into a luminophore bound to the product, wherein the mass label is capable of binding specifically to the substrate, and wherein the luminescence property of the luminophore is different for the luminophore bound to the product than for a complex of the luminophore, the substrate, and the mass label (col. 25, lines 30-36).

2. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pollok et al., 6,410,255.

Pollok et al. teach the invention substantially as claimed (see above). However, Pollok et al. do not teach that the luminophore is capable of having a photoluminescence lifetime that is greater than the rotational correlation time of the unbound luminophore and less than the rotational correlation time of the complex formed by binding of the substrate or the product to the mass label.

However Pollok et al. teach that once an optical probe is separated from the bead, this results in an increased rotational flexibility (col. 25, lines 32-36.) Pollok et al. teach that various choice of fluorescent moieties may be used (col. 7, lines 2-12.) Pollok et al. also teach that various choice of enzymes and substrates may used (col.

19, lines 18-27.) Whether the photoluminescence lifetime is greater than the rotational correlation time of the unbound probe (luminophore) and less than the rotational correlation time of the complex formed by binding of the substrate to the mass label depends on what fluorescent moiety is used and what choice of enzymes and substrates are used, and Pollok et al. teach that various choices of fluorescent moieties and enzymes and substrates may be used. Moreover, the photoluminescence lifetime as claimed by Applicant appears to be an optimum or workable range. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

3. Claim 33 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pollok et al., 6,410,255, in view of Zarling et al., 5,674,698.

Pollok et al. teach the invention substantially as claimed (see above). However, Pollok et al. do not teach that the mass label includes a plurality of binding moieties that bind to the substrate such that the mass label is capable of specifically binding to more than one substrate or product molecule at the same time.

Zarling et al. teach that more than one probe, such as antibodies, may be attached to a label, such as a bead, in polarization assays (col. 10, lines 53-57.) Zarling et al. teach that attachment chemistries can be employed to link the probe to the label (col. 10, lines 53-57.) It would have been obvious to one of ordinary skill in the art at the

time the invention was made to provide multiple binding moieties on the particle as taught by Zarling et al. in the Pollok et al. because Zarling et al. teach that more than one probe may be attached to a particle as an alternative to one probe per particle. (That is, Zarling et al. teach that one probe per particle is a functional equivalent to multiple probes, and thus multiple binding moieties, per particle.)

4. Claim 84 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pollok et al., 6,410,255, in view of Kopf-Sill et al., 6,524,790.

Pollok et al. teach the invention substantially as claimed (see above). More specifically, Pollok et al. teach that the mass label is a bead (col. 25, line 32). However, Pollok et al. do not teach that the material forming the bead is glass but only teaches that the solid matrix may be a bead in general.

Kopf-Sill et al. teach that solid supports such as beads, including glass beads, are suitable supports for immobilization of assay components such as peptides (col. 34, lines 54-61). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use glass as taught by Kopf-Sill et al. as the particular material for the beads generally disclosed Pollok et al. invention because Kopf-Sill et al. teach that glass beads are suitable types of beads for immobilization of assay components such as peptides, such as the peptides in the Pollok et al. invention.

5. Claims 83 and 34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yguerabide et al., 6,586,193, in view of Pollok et al., 6,410,255.

Yguerabide et al. disclose the invention substantially as claimed.

As to claim 83, Yguerabide et al. disclose a kit comprising:

an enzyme (col. 86, line 66 – col. 87, line 8);

and a particulate mass label including a bead (col. 12, line 32 and 40 and figure 30A) distinct from the enzyme and capable of specifically binding to the substrate or a product of the substrate produced by action of the enzyme on the substrate, but not both (col. 86, line 66 – col. 87, line 8)

Yguerabide et al. however do not teach a luminophore bound to the substrate for the enzyme, wherein a luminescence property of the luminophore is sensitive to binding of the mass label to the substrate or product.

Pollok et al. however teach that polarization measurements of a fluorescent moiety attached to an enzyme substrate which is immobilized on a bead are used to measure the rate of the enzyme-substrate activity (col. 25, lines 1-12, and lines 30-36.) Pollok et al. teach that cleavage of the substrate from the bead by the enzyme results in a larger drop in fluorescence polarization because of the increased rotational flexibility of the substrate once separated from the bead (col. 25, lines 32-36.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide attach a fluorescent moiety to the enzyme substrate as taught by Pollok et al. in the Yguerabide et al. because Pollok et al. teach that the

fluorescent moiety provides a means to detect the change in polarization once the substrate-fluorescent moiety is cleaved from the bead.

As to the following claims, Yguerabide et al. teach the limitations as follows.

As to claim 34, Yguerabide et al. teach that the mass label is a first mass label, the kit further comprising a second mass label capable of specifically binding to at least one of the substrate, a complex formed by binding of the luminophore to the substrate, the product, and the first mass label, but not to the luminophore alone (col. 12, lines 30-33, col. 84, lines 26-36, and col. 87, lines 61-64). (That is, Yguerabide et al. teach that linking two or more particles together using chemical or biological cross-linking agents amplifies detection of analytes.)

As to claim 35, Yguerabide et al. teach that the second mass label is capable of specifically binding to at least two first mass labels, so that the second mass label may form crosslinks between molecules of the substrate (col. 88, lines 3-12). That is, Yguerabide et al. teach that a particle aggregate or network structure that contains many particles bound together produces a high level of intensity which is much easier to detect than one particle" (col. 88, lines 3-12).

As to claim 36, Yguerabide et al. teach that the second mass label includes at least biotin (col. 88, lines 3-12). (The Office notes that although Yguerabide et al. teach that the second mass label includes biotin indirectly, through linkage with streptavidin, the claim nevertheless read on this disclosure.)

Response to Arguments

Applicants' arguments filed October 20, 2006 have been fully considered but are not persuasive.

Applicants argue on page 11 that in Pollok et al., both the substrate of the protease (intact polypeptide) and one of the cleavage products produced by action of the protease on the polypeptide remain attached to the bead during and accordingly, Pollok et al. disclose a bead attached to both a substrate and a product of the substrate, which is in contrast to claim 83 which recites a particulate mass label capable of specifically binding to the substrate or a product of the substrate produced by action of the enzyme on the substrate, but not both.

This argument is not persuasive because Applicants' claims do not exclude the disclosure of Pollok et al. That is, Applicants do not recite to *which* cleavage products produced by action of the protease on the polypeptide is being referred in claim 83. Applicants rather claim that the particulate mass label is capable of specifically binding to the substrate or a product of the substrate produced by action of the enzyme on the substrate. As acknowledged by Applicants, there are two cleavage products. One cleavage product remains attached to the bead and the other does not. To meet Applicants' limitation at issue, the bead only needs to be capable of specifically binding to the substrate, i.e., the polypeptide, (or a product), but not both the substrate, i.e., the polypeptide, and the product. The product as claimed by Applicant is deemed to be the cleavage product that does not remain attached to the bead once the polypeptide is

cleaved by the enzyme. It is noted that Applicants also do not recite that the particulate mass label is not capable of binding to the substrate and both of the cleavage products. Thus, Applicants' claimed invention is not distinguished over the Pollok et al. prior art reference.

Applicants also make the same argument on pages 11-12 for the rejection under Yguerabide et al. in view of Pollok et al., stating that in Pollok et al., the light scattering particle is attached both to the substrate and to a product of the substrate produced by cleavage of the substrate, which is in contrast to claim 83. The argument is not persuasive for the same reasons as set forth above, namely that the cleavage product that does not remain attached to the particle after cleavage is considered to be the claimed "product".

Applicants also argue that with respect to the rejections using the Nikiforov reference, the reference does not constitute prior art to Applicants' earliest filing date for the subject matter of claim 83. The rejection under Nikiforov has been withdrawn. It is noted that claim 88 (formerly rejected under Nikiforov) is now rejected under Pollok et al. (see above).

Applicants also argue on page 14 that none of the reference disclose a first and second mass label capable of specifically binding to at least two first mass labels. This is not persuasive because, as indicated above in the grounds of rejection, Yguerabide et al. disclose this in column 12, lines 3-33 and column 84, lines 26-36, and column 87, lines 61-64. (Yguerabide et al. teach that linking two or more particles together using chemical or biological cross-linking agents amplifies detection of analytes.) Applicants

also argue that the references also do not disclose a second mass label including "avidin, biotin, lectin, sugar, an immunological binding partner, or a combination thereof" as recited by claim 36. This is not persuasive because, as indicated above in the grounds of rejection, Yyguerabide et al. disclose this in column 88, lines 3-12 (the solid-phase and biotin are considered to be the second mass label.)

It is acknowledged that Applicants' attorney stated that the IDS filed November 7, 2005 as well as the foreign priority document filed November 7, 2005 does not belong to the present application and request that these documents be removed from the application file of the present application. These documents have now been removed from Applicants' file.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ANN YEN LAM
PATENT EXAMINER